REMARKS

In this response to the Office Action dated July 22, 2010, Applicants have amended Claims 21, 28, 33 and 35-37. Support for the amendment to Claim 21 can be found, for example, from page 1, line 27 (the last line) to page 2, line 3 of the specification as originally filed. Support for the amendment to Claim 33 can be found, for example, from Table 1. (Staining Procedure), Example 1, and Figures 2 and 4 of the specification. Claims 35-37 have been amended to properly recite the antecedent basis. Claims 31 and 34 have been canceled without prejudice. No new matter is added in these amendments. Upon entry of the amendments, Claims 21, 26-30, 32, 33 and 35-37 are pending.

In light of the amendments and remarks as set forth herein, Applicants respectfully request withdrawal of the claim rejections and consideration of pending claims for the patentability.

Rejection of Claims 33 and 37 under 35 U.S.C. 112, first paragraph

Claims 33 and 37 were rejected under 35 U.S.C. 112, first paragraph, as allegedly failing to comply with the enablement requirement. The Examiner asserted that one would expect antibodies specific to NC1 to bind to NC1 in the glomerular basement membranes of kidney samples regardless of whether the subject mammal providing the sample suffered from nephritis or not in view of Johansson et al. (J. Biol. Chem. 267: 24553, 1992).

As stated by the Examiner, the foregoing rejection was previously made with regard to the prior similar subject matter of Claims 25 and 29. In response to the current rejection of Claims 33 and 37, Applicants provides arguments similar to what were presented and resulted in overcoming the prior rejection of Claims 25 and 29.

The antibody of Claims 33 and 37 exhibits substantially more binding to a frozen kidney tissue obtained from a mammal with nephritis as compared to that obtained from a normal mammal. The selection of such a monoclonal antibody is illustrated in Example 1 of the specification as filed. The specification also provides experimental evidence showing this specific binding of anti-NC1 monoclonal antibody to a nephritis-conditioned sample. For example, as presented in Figure 2, the anti-NC1 monoclonal antibody shows a significantly and noticeably higher binding to the nephritis model kidney (lower panel) than the normal control kidney (upper panel). Such a noticeably distinctive affinity of the cited antibody to a sample with the disease condition would allow a user to readily identify the sample under condition of

nephritis. In addition, to more explicitly define the specificity of the cited antibody, Claim 33 as amended further recites the features that are related to Applicants' selection process of the cited antibodies.

In view of the foregoing remarks and amendments, Applicants respectfully submit that Claims 33 and 37 are in compliance with the enablement requirement, and therefore request withdrawal of the rejection.

Rejection of Claims 27 and 28 under 35 U.S.C. 112, first paragraph

Claims 27 and 28 were rejected under 35 U.S.C 112, first paragraph, as allegedly failing to comply with the enablement requirement.

In this rejection, the Examiner appears to view that the present disclosures teach a method for determination of antigen-antibody binding only in a fluid sample, not in a frozen tissue sample. According to this view, the Examiner asserted that one would have no assurance of practicing the methods as claimed in Claims 27 and 28, which are directed to the method applicable to a frozen tissue sample, because one would not be able to apply a method taught as suitable for fluid samples to a frozen tissue sample.

Applicants respectfully note that the present application provides explicit disclosures of the method of identifying presence of nephritis in a frozen tissue sample. For example, Table 1 in page 12 of the specification as originally filed discloses detailed information of a staining procedure for determining antigen-antibody binding in a frozen renal tissue. Furthermore, the data shown in Figure 2 demonstrated the effective staining results obtained with the monkey kidney samples after following the protocol of Table 1. In addition, Claim 28 as amended specifically recites the techniques of immunohistochemistry as explicitly taught in connection with Table 1.

In view of the foregoing remarks and amendments, Applicants respectfully submit that Claims 27 and 28 are in compliance with the enablement requirement. Therefore, Applicants respectfully request withdrawal of the rejections.

Rejection of Claims 21 and 26-37 under U.S.C. 112, first paragraph

Claims 21 and 26-37 were rejected under 35 U.S.C. 112, first paragraph, as allegedly failing to comply with the enablement requirement. More particularly, the Examiner asserted that absent any showing of the timing of the appearance of significant levels of the epitope detected by the NC1 monoclonal antibody, it would seem unknown and unpredictable that the

antigen (or the particular epitope) would be detectable at detectably different levels in a mammal with early stage disease and not only after disease has manifested in the hosts, i.e. at injury crisis as exemplified in the specification. The Examiner further asserted that absent further guidance for applicant, one would not be assured of the predicable ability to perform the method as is now claimed with kidney tissue samples.

Applicants respectfully submit that the specification as filed provides evidence showing that the currently claimed method can detect the nephritis condition at an early stage of the disease with a kidney tissue sample. As further described in the accompanying Declaration and Exhibit A, a patient having a renal disease generally does not show any signs indicating the disease condition at the early stages of the disease. Among the five stages of the renal disease that are defined by the U.S. National Kidney Foundation, the early stages such as Stages 1 and 2 generally show no obvious change in glomerular filtration rate (GFR) and serum creatinine levels, which are commonly used indexes to determine the disease progression. Further, the pathological signs such as deposition of Ig and glomerular crescent formation are hardly observed in the patient's renal tissue at Stages 1 and 2. Therefore, it is very difficult to diagnose the disease at the early stages.

Applicants showed in the instant application (e.g. Figure 4) that the method according to the pending claims can identify presence of the disease in a human kidney sample that had the renal disease but was devoid of any pathological signs (i.e. deposition of immunoglobulin (Ig) and glomerular crescent formation). In the test shown in Figure 4, Applicants applied the method to a sample with minimal change type of nephritis (shown in panel 3 of Figure 4) and compared the result with those obtained from the positive controls (shown in panels 1 and 2). In general, the minimal change type of nephritis does not show Ig deposition and/or renal crescent and further the patient's renal tissue generally appears normal and healthy. Thus, the detection of this disease is quite difficult. However, as clearly demonstrated in Figure 4, Applicants' method generated the positive signals from the sample of minimal change type of nephritis and the signals are highly comparable to those obtained from the positive controls. Moreover, when the method was applied to the sample of the same disease after treatment, the positive signals significantly disappeared. These data clearly demonstrate that Applicants' method can detect the presence of the renal disease condition even before any pathological signs (e.g. Ig deposition/renal crescent formation) are developed. Accordingly, the method is clearly suitable

for detecting the renal disease at the early stages of the disease when there is no substantial sign of the disease is apparent.

In view of the foregoing, Applicants believe that the subject matter of the pending claims is in compliance with the requirements under 35 U.S.C. 112, first paragraph. Accordingly, withdrawal of the rejection and reconsideration of the pending claims is respectfully requested.

Rejection of Claims 35-37 under U.S.C. 112, second paragraph

Claims 35 -37 were rejected under 35 U.S.C 112, second paragraph, as being indefinite. More particularly, the claims were rejected for lacking antecedent basis. In response, Applicants have amended Claims 35-37 as set forth above. In view of the amendments, the claims properly recite the antecedent basis and, accordingly satisfy the requirements of 35 U.S.C 112, second paragraph. Withdrawal of the rejection is therefore respectfully requested.

No Disclaimers or Disavowals

Although the present communication may include alterations to the application or claims, or characterizations of claim scope or referenced art, Applicants are not conceding in this application that previously pending claims are not patentable over the cited references. Rather, any alterations or characterizations are being made to facilitate expeditious prosecution of this application. Applicants reserve the right to pursue at a later date any previously pending or other broader or narrower claims that capture any subject matter supported by the present disclosure, including subject matter found to be specifically disclaimed herein or by any prior prosecution. Accordingly, reviewers of this or any parent, child or related prosecution history shall not reasonably infer that Applicants have made any disclaimers or disavowals of any subject matter supported by the present application.

CONCLUSION

In view of Applicants' foregoing Amendments and Remarks, it is respectfully submitted that the present application is in condition for allowance. Should the Examiner have any remaining concerns which might prevent the prompt allowance of the application, the Examiner is respectfully invited to contact the undersigned at the telephone number appearing below.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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Dated: January 24, 2011

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